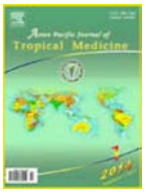
Contents lists available at ScienceDirect

Asian Pacific Journal of Tropical Medicine

journal homepage:www.elsevier.com/locate/apjtm



Document heading doi: 10.1016/S1995-7645(14)60200-5

A review on most important herbal and synthetic antihelmintic drugs

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ARTICLE INFO

Article history:
Received 3 Jun 2014
Received in revised form 25 Aug 2014
Accepted 20 Sep 2014
Available online 27 Sep 2014

Keywords:
Herbal medicine
Medicinal plant
Antihelmintic drugs
Antinematoda
Anticestoda

ABSTRACT

Parasites and parasitic diseases are widely spread in the world. Their adverse effects on health and social-economic society cause tremendous public health problems. Parasitic infections in different ways (water, soil, food and vegetables) can affect humans and induce other complications such as gastrointestinal disorders, malnutrition, anemia and allergies and sometimes even life threatening. Medicinal plants are being widely used, either as a single drug or in combination with synthetic drugs. These medicinal plants are considered as a valuable source of unique natural products and drugs for development of medicines against various disorders and diseases. In this article the recently published papers about medicinal plants and parasites were reviewed, using scientific sites such as Medline, PubMed and Google Scholar. The used terms included: herbal medicine, medicinal plants, and antihelmintic drugs, antinematoda, anticestoda, antitrematoda. From the above collected literature it might be concluded that these plants are promising potential sources for preparation of new drugs or for pharmacological and therapeutic applications.

1. Introduction

Parasites and parasitic diseases are widely spread in the world. Their adverse effects on health and social-economic society are more visible and has been considered in some areas of Iran with tremendous public health importance. Parasitic infections in different ways (water, soil, food and vegetables) can affect humans and induce other complications such as gastrointestinal disorders, malnutrition, anemia and allergies and sometimes even life threatening[1,2].

Worms are in three categories, Nematoda, Cestoda and Trematoda. For these three categories, three groups of drugs are available.

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Foundation project: Supported by Deputy for Research and Technology of Lorestan University of Medical Sciences, research grant (No. 224).

2. Antinematoda, Anticestoda and Antitrematoda drugs

Antinematoda drugs against pinworm, hookworms, *Ascaris* and *Strongyloides* include piperazine, mebendazole, thiabendazole, pyrantel, ivermectin and diethyl carbamazine. Antitrematoda drugs include praziquantel, bithionol sulfoxide, oxamniquine, metrifonate. The third group of antihelminths are anticestoda such as niclosamide which are applied agaist tapeworms such as *Taenia*, *Echinococcus* and *Diphyllobothrium*[3]. Levamisole is an antibiotic which is often prescribed as anti-parasitic drugs against nematodes such as *Ascaris*, tricostrongyloids and various hooked worms[3].

Albendazole mechanism of action is degeneration of cytoplasmic microtubules in parasite cells[3]. Praziquantel increases cell membrane permeability to calcium, causing cup muscle paralysis, resulting in removing from

the vessel wall[3]. Mebendazole causes immobility and death of the worms by selectively inhibiting irreversible absorption of glucose. Mebendazole has not good intestinal absorption after excessive use and is found unchanged in the feces[3]. Niclosamide can inhibit oxidative phosphorylation in mitochondria of flat worms, resulting in worm death[3]. Thiabendazole is a benzimidazole that can inhibit anaerobic metabolism and damage microtubule of the parasite[3], and prevents tubulin polymerization and microtubules creation in parasite cells. Microtubules have a main role in building cellular cytoskeleton[3]. Quinine is obtained from *Cinchona* bark and has anti-inflammatory effects in addition to degradation ability of *Plasmodium*. Quinine is an alkaloid with accumulation ability in acidic vesicles of malaria parasites which causes cells death because of changing intracellular pH[3].

The main use of diethylcarbamazine drug is used in treating some parasitic diseases such as lymphatic filariasis (elephantiasis). These drugs inhibit the metabolism of arachidonic acid in nematodes that cause lymphatic filariasis (*Wuchereria bancrofti*, *Brugia malayi*, *Loa loa*, *etc.*)[3]. Dehydroemetine is used to treat for *Fasciola hepatica* infection. Its mechanism action is not clear exactly, but probably is effective on cell proliferation[3]. Pyrvinium pamoate inhibits oxygen uptake and use of exogenous carbohydrates in aerobic parasites[3]. At present lymphatic filariasis is treated with diethylcarbamazine and ivermectin or in combination with Albendazole[4].

Drug-resistant is the main problem in parasite therapy. Hence, new drugs are urgently needed[5]. At present time many medicinal plants have been studied in traditional medicine including Ayurveda and Chinese medicine. On the other hand a number of promising drugs or natural products have been identified not only in eradication of parasites[6-8], but also in treating other infective[9-11], and none infective diseases[12-15]. Studies have shown that *Streblus asper* from the Moraceae family has anti-filarial activity[8]. Onchocerciasis is treated with ivermectin in combination with albendazole, which are not known to treat dracunculiasis[4]. The number of plants which have been tested against onchocerciasis and dracunculiasis are much less than filariasis, but a few African plants have been recorded in this regard[16].

Medicinal herb extracts have examined in most studies and phytochemical profiles of secondary metabolites have been published.

Schistosomiasis has also treated with praziquantel alone or in combination with albendazole or ivermectin. Also oxamniquine and anti-malarial drugs such as artemisinin and quinoline alkaloids and its derivatives are used[4]. Anthraquinones in *Rheum palmatum* and *Rumex dentatus* (Polygonaceae) and phorbolesters from *Jatropha curcas* (Euphorbiaceae) had molluscicidal activity against schistosomias vector snails *Oncomelania*, *Biomphalaria* and *Bulinus*[17].

Antihelminthic drug compounds have also been obtained from plants including arecoline, pelletierine, filixic acid, ascaridole, aspidin and curcumin (Figure 1)[18].

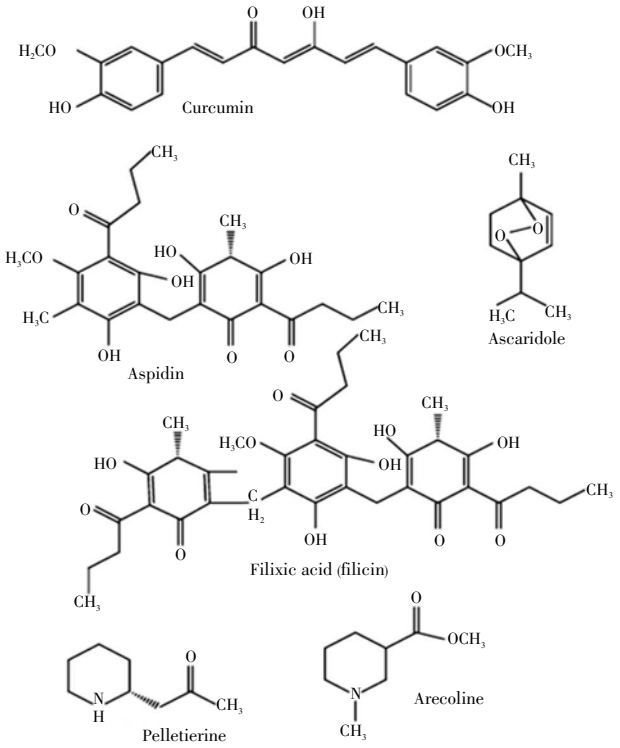

Figure 1. Chemical structures of arecoline, pelletierine, filixic acid, ascaridole, aspidin and curcumin.

Curcumin extracted from turmeric have anti-parasitic effects against schistosoma[18]. Ascaridole is another antihelmintic compound isolated from *Chenopodium* plant[19]. Ascaridole is an effective drug against hookworm infection, but it is mutagenic and toxic[20]. Another traditional herb is the fern *Dryopteris filix-mas* (Dryopteridaceae) which contains vermicidal phloroglucinols, such as aspidin, deaspidin, and filixic acid (syn. filicin). They are active against intestinal cestodes and probably paralyze the worm's muscles[21]. However, this drug has considerable side effects for humans but filixic acid is used as an anthelmintic in veterinary praxis.

Other paralyzed agents are the anthelmintic alkaloids such as pelletierine from *Punica granatum* (Lythraceae) and arecoline from *Areca catechu* (Arecaceae), which target acetylcholine receptors[20]. Other anthelmintic plants include *Artemisia maritima* (with santonin), *Artemisia abrotanum* (Asteraceae), *Zanthoxylum liebmannianum* (Rutaceae), *Thymus vulgaris* (Lamiaceae), *Millettia thonningii*, *Albizia anthelmintica*, *Butea frondosa* (Fabaceae), *Embelia schimperi* (Myrsinaceae), *Teloxys graveolens* (Amaranthaceae) and several others such as: *Punica granatum*, *Allium sativum*, *Cucurbita maxima* and *Cucurbita pepo*, *Polypodium vulgare*, *Aspidium filix-mas*,

Pleurotus eryngii, Delphinium consolida, Ruta graveolence, Fraxinus excelsior, Berberia spp., *Artemia salina, Artemisia inculata, Artemisia abyssinica, Artemisia absantin, Albizia grandibracteata, Ficus exasperata, Zygophyllum album, Zygophyllum coccineum, Citrullus colocynthis, Artemisia vulgaris, Calamintha nepeta, Datura stramonium, Nerium oleander, Nicotina tabacum, Pteridium aquilinum, Sambucus nigra, Tanacetum vulgare, Artemisia abrotanum, Salvia officinalis, Zingiber officinale, Allium sativum, Olea europaea*[22-29].

Nicotin is another antihelminth compound (Figure 2). *Nicotiana tabacum* (Tobacco) contains the alkaloid nicotine, nicoteine, nicotelleine, nicotimin mainly in leaves. These substances are highly toxic but the main effect of them is anti-parasitic effect[30].

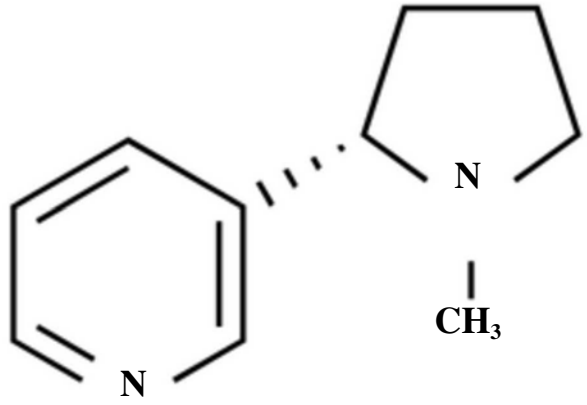

Figure 2. Nicotin chemical structure.

Mallotus philippensis plant or kamala tree grows in Asia and Australia regions and its fruits or extracts have strong antihelminthal effect. It is used to treat infection with *Bothriocephalus* in carp fish[30].

Agrimophol is a vermicide drug obtained from *Agrimonia eupatoria* L. plant. Arecoline is a herbal remedy obtained from *Areca catechu*. Kainic acid material is an anti-ascaris drug witch obtained from *Digenea simplex* plant. Quisqualic acid is another herbal vermicide drug obtained from Quisqualic indica L. plant. Santonin as an anti-ascaris drug obtained from *Artemisia maritima*[31].

3. Reliability of medicinal plants

As it was mentioned medicinal plants and their bioactive ingredients not only are anti-helminthic, but also are used to treat most serious, metabolic and functional diseases such as viral[9], and bacterial infections[32-34], hyperlipidemia[35-38], diabetes[39-42], atherosclerosis[43-46], neurological disorders[47-50], cancer[51-54], wound healing[55-58], gastrointestinal disorders[59-61], and are reliable resources for production and supply of effective drugs with less side effects and low toxicity[62-65].

4. Conclusion

Medicinal plants are being widely used, either as a single drug or in combination delivery system and these herbal plants are considered as a valuable source of unique natural products and drugs against various disorders and diseases and also for development of industrials products.

From the above collected literature it might be concluded that these plants are promising potential sources for preparation of new drugs or for pharmacological and therapeutic applications.

Conflict of interest statement

We declare that we have no conflict of interest.

Acknowledgements

This research was supported by research grant (No. 224) from Deputy for Research and Technology of Lorestan University of Medical Sciences.

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